Chemical Risk Assessment at the Occupational Safety and Health Administration

Although the Occupational Safety and Health Administration (OSHA) generally follows the standard four-step National Academy of Sciences' (NAS) paradigm for risk assessment, there are several distinguishing characteristics of its assessments. Under its statutory mandate, OSHA has a specific and narrow focus on the potential risks to workers in an occupational setting. Further, the underlying statute and court decisions interpreting the statute have required the agency to focus on demonstrating, with substantial evidence, that significant risks to workers exist before it can regulate. In addition to presenting its own best estimates of risk, OSHA may present estimates based on alternative methods and assumptions.

Context for OSHA Chemical Risk Assessment

Much of what is distinct about risk assessment at OSHA can be traced to statutory provisions, court decisions, and the nature of workplace exposures to chemicals. OSHA, an agency within the Department of Labor, was created by the Occupational Safety and Health Act of 1970 (the OSH Act).[1] The central purpose of the act is to ensure safe and healthful working conditions. As one of the primary means of achieving this goal, the act authorizes the Secretary of Labor to promulgate and enforce mandatory occupational safety and health standards.[2] Certain provisions in the act stipulate both the nature and the manner in which these standards should be established. For example:

- Under section 3(8) of the OSH Act, a safety or health standard is defined as a standard that requires conditions, or the adoption or use of one or more practices, means, methods, operations, or processes, reasonably necessary or appropriate to provide safe or healthful employment or places of employment.
- According to OSHA, a standard is reasonably necessary or appropriate within the meaning of section 3(8) if it eliminates or substantially reduces significant risk and is economically feasible, technologically feasible, cost effective, consistent with prior OSHA action or supported by a reasoned justification for departing from prior OSHA actions, supported by substantial evidence on the record as a whole, and is

[1] 29 U.S.C. 651 *et seq.*

[2] Safety standards are generally designed to reduce on-the-job injuries. Health standards are usually directed at limiting the risk of workers developing occupational diseases from exposure to hazardous chemical or physical agents.

better able to effectuate the act's purposes than any national consensus standard it supersedes.

- Section 6(b)(5) of the act states that "The Secretary, in promulgating standards dealing with toxic materials or harmful physical agents... shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life."

A significant factor influencing the interpretation of the OSH Act provisions and OSHA's approach to risk assessment is the Supreme Court ruling in its 1980 "Benzene" decision that, before issuing a standard, OSHA must demonstrate that the chemical involved poses a "significant risk" under workplace conditions permitted by current regulations and that the new limit OSHA proposes will substantially reduce that risk.[3] This decision effectively requires OSHA to evaluate the risks associated with exposure to a chemical and to determine that these risks are "significant" before issuing a standard. However, the court provided only general guidance on what level of risk should be considered significant. The court noted that a reasonable person might consider a fatality risk of 1 in 1000 (10^{-3}) to be a significant risk and a risk of one in one billion (10^{-9}) to be insignificant. Thus, OSHA considers a lifetime risk of 1 death per 1,000 workers to represent a level of risk that is clearly significant. The court also stated that "while the Agency must support its findings that a certain level of risk exists with substantial evidence, we recognize that its determination that a particular level of risk is significant will be based largely on policy considerations."[4]

Later Court of Appeals decisions have interpreted the Supreme Court's "Benzene" decision to mean that OSHA must quantify or explain the risk for each substance that it seeks to regulate unless it can demonstrate that a group of substances share common properties and pose similar risks.[5] Although this decision does not require OSHA to quantitatively estimate the risk to workers in every case, it does preclude OSHA from setting new

[3] *Industrial Union Dept. v. American Petroleum Inst.*, 448 U.S. 607, 642 (1980).

[4] 448 U.S. at 655-56 n.62.

[5] *AFL-CIO v. OSHA*, 965 F.2d 962 (11th Cir. 1992), *International Union, UAW v. Pendergrass*, 878 F.2d 389 (D.C. Cir. 1989).

standards without explaining how it arrives at a determination that the standard will substantially reduce a significant risk.

According to OSHA officials, the other important contextual influence on OSHA risk assessment is the very nature of workplace exposures to chemicals. Generally, workplace exposures to chemicals are at higher levels than most environmental exposures to chemicals experienced by the general public. Workers are often exposed to many chemical agents at levels not much lower than those used in experimental animal studies. According to agency officials, this is one of the unique features of OSHA's chemical risk assessments. Also, OSHA frequently has relevant human data available on current exposures, in contrast to most other agencies regulating toxic substances.

Risk Assessment Procedures

General Approach

OSHA currently has no formal internal risk assessment guidance. Instead, OSHA has primarily described its general risk assessment methods, as well as the rationale for specific models and assumptions selected, in the record of each risk assessment and regulatory action. One reason for this, according to agency officials, is that OSHA performs risk assessments only for its standards. Overall, they said the agency only publishes two or three proposed or final rules per year, and not all of these rules involve a chemical risk assessment. The officials also emphasized the incremental nature of advances in risk assessment methods and science, with successive assessments establishing precedents for methods that may be used for succeeding analyses.

Like EPA and FDA, OSHA uses the basic NAS four-step process for risk assessment. Another fundamental source for OSHA's (and EPA's and FDA's) methods was the 1985 document on chemical carcinogens produced by the Office of Science and Technology Policy.[6] OSHA often refers to the reference sources of other entities, including other federal agencies, in

[6] Office of Science and Technology Policy, Executive Office of the President, "Chemical Carcinogens: A Review of the Science and Its Associated Principles, February 1985," 50 FR 10372 (Mar. 14, 1985).

both specific rulemakings and as general technical links to its on-line information on occupational risks.

Despite these common elements and procedures, several features of OSHA's approach differ from those of other federal agencies. Because OSHA does not currently have written internal guidance on its risk assessment procedures, the information in the following sections is derived primarily from an examination of OSHA's chemical risk assessments.[7] We also relied on secondary sources, such as Lorenz Rhomberg's report on federal agencies' risk assessment methods.[8]

Hazard Identification

In OSHA's risk assessments, the hazard identification step results in a determination that an exposure to a toxic substance causes, is likely to cause, or is unlikely or unable to cause, one or more specific adverse health effects in workers. According to OSHA, this step also shows which studies have data that would allow a quantitative estimation of risk. OSHA defines hazardous and toxic substances as those chemicals present in the workplace that are capable of causing harm. In this definition, the term chemicals includes dusts, mixtures, and common materials such as paints, fuels, and solvents. OSHA currently regulates exposure to approximately 400 such substances. In the workplace environment, chemicals pose a wide range of health hazards (e.g., irritation, sensitization, carcinogenicity, and noncancer acute and chronic toxic effects) and physical hazards (e.g., ionizing and nonionizing radiation, noise, and vibration).

[7] Because OSHA's methylene chloride standard is the most recent hazardous chemical rulemaking, most of the specific examples cited come from OSHA's methylene chloride rulemaking: "Occupational Exposure to Methylene Chloride," 62 FR 1494 (Jan. 10, 1997).

[8] Lorenz R. Rhomberg, *A Survey of Methods for Chemical Health Risk Assessment Among Federal Regulatory Agencies*, a report prepared for the National Commission on Risk Assessment and Risk Management (1996).

Most of OSHA's chemical risk assessments have addressed occupational carcinogens. In assessing potential carcinogens, OSHA may consider the formal hazard classification or ranking schemes of other entities as part of the available evidence on a particular chemical. Ultimately, though, OSHA makes its own determinations on the risk posed by particular compounds and their classification as potential occupational carcinogens. OSHA's chemical risk assessments may also discuss noncancer hazards. For example, in the final rule on methylene chloride the agency discussed the evidence regarding central nervous system, cardiac, hepatic (liver), and reproductive toxicity, as well as carcinogenicity. Similarly, the agency's rulemaking on 1,3-butadiene addressed adverse health effects such as developmental and reproductive toxicity and bone marrow effects in addition to the evidence on carcinogenicity.[9] OSHA quantifies the risks of noncancer effects if it determines that there are adequate data on exposure and response for the substance of interest.

OSHA officials also noted that OSHA has a hazard communication standard, which requires manufacturers, shippers, importers, and employees to inform their employees of any potential health hazard when handling these chemicals. This is usually done through container labeling and material safety data sheets. Although this standard does not address specific risks posed by individual chemicals, it is a comprehensive hazard information standard for nearly all chemicals in commerce.

Dose-Response Assessment

Carcinogens

OSHA's general procedures for dose-response assessment are similar to those of EPA and FDA, especially in the choice of data sets to use for quantitative assessments. However, OSHA probably uses a linear low-dose extrapolation model less often than is the case for other agencies. OSHA differs from the other federal regulatory agencies also in being less conservative in setting its target risk levels when conducting low-dose extrapolation. As previously noted, the main points of OSHA's risk assessments for regulatory purposes are to determine whether significant risks exist and to demonstrate in a broad sense the degree to which the standard would reduce significant risk. The specific choice of where to set

[9] "Occupational Exposure to 1,3-Butadiene" 61 FR 56746 (Nov. 4, 1996).

the standard is tempered by the statutory mandate that standards must be technologically and economically feasible.

Like other agencies, OSHA states that, all things being equal, epidemiological data are preferred over data from animal studies whenever good data on human cancer risks exist. More often than some other agencies regulating exposures to toxic substances, OSHA may have relevant human data on adverse health effects available for consideration in its risk assessments. However, the rulemaking examples we reviewed also illustrate that these epidemiological data may be considered inadequate for quantitative dose-response assessment, while animal data may provide more precise and useful dose-response information. In both the methylene chloride and 1,3-butadiene dose-response assessments, for example, OSHA had both epidemiological and animal data available, but based its quantitative estimates on data from rodent models. However, OSHA did use its analysis of the epidemiological data when examining the consistency of the results derived from animal studies.

When faced with the choice of several animal data sets, OSHA tends not to combine tumor sites but to choose the data set showing the highest sensitivity (i.e., most sensitive sex, species, and tumor site). The agency will, however, frequently present information from alternative data sets and analyses. The agency is likely to include benign tumors with the potential to progress to malignancy along with malignant tumors in the data set used for its quantitative assessments. OSHA cited the Office of Science and Technology Policy's views on chemical carcinogens in support of this practice, as well as noting that other federal agencies, including EPA and FDA, have also included benign responses in their assessments.

Because occupational exposures tend to be closer to the range of experimentally tested doses in animal studies, extrapolation may pose less of a challenge for OSHA than for other regulatory agencies. OSHA's preferred model for quantitative analysis of animal cancer dose-response data and for extrapolation of these data to low doses is the "multistage model," which is based on the biological assumption that carcinogens induce cancer through a series of independent ordered viable mutations, and that cancer develops through stages. Unlike EPA and FDA, however, OSHA tends to focus on the maximum likelihood estimate (MLE) of the fitted dose-response curve rather than on an upper bound, although the agency also provides estimates for the 95-percent upper confidence limit (UCL) of the dose-response function. This procedure generally leads to a less conservative risk estimate than the procedures used by EPA or FDA.

Like EPA and FDA, OSHA generally assumes no threshold for carcinogenesis. In contrast to the other agencies, OSHA's default dose-metric for interspecies extrapolation is body weight scaling (mg/kg/day – i.e., risks equivalent at equivalent body weights). According to OSHA, this default is used to be consistent with prior chemical risk assessments, but it also reflects a conscious policy decision that its methodology should not be overly conservative. OSHA says it may in the future move to ¾ -power scaling, as agreed to by EPA, FDA, and the Consumer Product Safety Commission some years ago. OSHA also says it is currently considering developing a different form of the multistage model, which will provide more stable MLE estimates than does the current form.

OSHA also considered data from physiologically based pharmacokinetic (PBPK) models in the risk assessment examples we reviewed.[10] PBPK models provide information on target organ dose by estimating the time distribution of a chemical or its metabolites through an exposed subject's system.[11] OSHA noted that PBPK modeling can be a useful tool for describing the distribution, metabolism, and elimination of a compound of interest under conditions of actual exposure and, if data are adequate, can allow extrapolation across dose levels, routes of exposure, and species. In particular, pharmacokinetic information is useful in modeling the relationship between administered doses and effective doses as a function of the exposure level.[12] However, PBPK models are complicated and require substantial data, which may not be available for most chemicals. OSHA pointed out in the methylene chloride rule that differences in the risk estimates from alternative assessments (including those submitted by outside parties) were not generally due to the dose-response model used, but to whether the risk assessor used pharmacokinetic modeling to

[10] Pharmacokinetics is the study of the absorption, distribution, metabolism, and elimination of chemicals in humans and animals. It is the basis for developing more realistic and accurate models of the movement and interactions of a chemical with blood, tissues, and organs once it enters the body, including consideration of the body's ability to repair damage caused by a chemical. PBPK models are based on the physiology of the exposed subjects, in contrast to more general compartmental pharmacokinetic models that do not necessarily represent effects on real anatomic regions/compartments of the body.

[11] Once in the body, a chemical may be chemically altered to form metabolites. Either the chemical itself or its metabolites may produce toxic effects. Therefore, both may need to be considered in assessing the potential harm associated with a given chemical.

[12] The administered dose is the amount of a substance given to an animal or human (e.g., through diet, drinking water, or ambient air). The effective dose is the amount that actually reaches a target organ or tissue.

estimate target tissue doses and what assumptions were used in that modeling.

In the methylene chloride standard, OSHA developed a set of 11 criteria to judge whether available data are adequate to permit the agency to rely on PBPK analysis in place of administered exposure levels when estimating human equivalent doses. Although it is beyond the scope of this appendix to provide a full technical explanation of the following criteria, they do illustrate the complex nature of PBPK analysis and, more generally, the types of issues that risk assessors consider in weighing the available data.

1. The predominant as well as all relevant minor metabolic pathways must be well described in several species, including humans.

2. The metabolism must be adequately modeled.

3. There must be strong empirical support for the putative mechanism of carcinogenesis.

4. The kinetics for the putative carcinogenic metabolic pathway must have been measured in test animals *in vivo* and *in vitro* and in corresponding human tissues at least *in vitro*.[13]

5. The putative carcinogenic metabolic pathway must contain metabolites that are plausible proximate carcinogens.

6. The contribution to carcinogenesis via other pathways must be adequately modeled or ruled out as a factor.

7. The dose surrogate in target tissues used in PBPK modeling must correlate with tumor responses experienced by test animals.

8. All biochemical parameters specific to the compound, such as blood:air partition coefficients, must have been experimentally and reproducibly measured. This must especially be true for those parameters to which the PBPK model is sensitive.

[13] The term *in vivo* refers to tests carried out within living organisms, while *in vitro* refers to tests outside the organism (e.g., using cells taken from an animal or human).

9. The model must adequately describe experimentally measured physiological and biochemical phenomena.

10. The PBPK models must have been validated with other data (including human data) that were not used to construct the models.

11. There must be sufficient data, especially data from a broadly representative sample of humans, to assess uncertainty and variability in the PBPK modeling.

In the 1,3-butadiene standard, which came out after the methylene chloride standard, OSHA used these same 11 criteria to judge the adequacy of the 1,3-butadiene PBPK models for dose-response assessment. In the butadiene case, the PBPK models did not meet all of these criteria.

For dose-response analyses from human cancer data, OSHA tends to use similar methodologies to the other regulatory agencies. Mostly these are simple linear models, such as relative risk models, and estimates of risk are based on the MLE.

Noncancer Effects

No specific approach or procedure for the assessment of noncancer effects was evident in the examples of OSHA rulemakings we reviewed. However, OSHA clearly considered a range of noncancer toxic effects in its analyses. In its rulemakings, OSHA focused on describing and analyzing a variety of relevant studies, case reports, and other information found in the scientific literature. Rhomberg noted that, in the past, OSHA used methods that were comparable to those of other agencies. However, the federal court in the *AFL-CIO v. OSHA* case questioned the use of standard safety factors, noting that "application of such factors without explaining the method by which they were determined... is clearly not permitted."[14]

OSHA has produced quantitative risk estimates for reproductive and developmental effects (glycol ethers, 1993), heart disease and asthma (environmental tobacco smoke, 1994), Hepatitis B virus infection (bloodborne pathogens, 1992), tuberculosis, and kidney toxicity from cadmium exposure. OSHA is currently working on quantitative risk assessments for such adverse health effects as cardiovascular disease mortality, neural effects, asthma, and respiratory tract irritation for a number of substances. OSHA states that new methodology has been used

[14] 965 F.2d at 978.

for these assessments, but review drafts were not yet ready and we cannot comment further.

Exposure Assessment

Under the OSH Act, OSHA has a relatively specific and narrow focus on exposure assessment. OSHA's primary focus is estimating the risk to workers exposed to an agent for a working lifetime. This risk is calculated in terms of a person exposed at a constant daily exposure level for 45 years at 5 days per workweek and 8 hours per workday. The goal is to set standards, in the form of permissible exposure limits (PELs), so workers would suffer no impairment during the course of their lifetime under a continuous exposure scenario. Although this is a hypothetical exposure scenario, Rhomberg observed that it is not conservative compared with the actual distribution of exposures in the workplace. He also noted that, in assessing the exposures and risks associated with the new proposed standard, OSHA assumes that the standard is applied to newly exposed workers who will work under the new standard for their entire working lives. No allowance is made for the fact that current workers may already have had exposures higher than the new standard.

Despite the primary focus on long-term working lifetime exposures, there may also be some risks posed by acute, short-term exposures. Therefore, although part of OSHA's risk assessment could focus on longer-term risks and deal with 8-hour time-weighted average (TWA) exposure, the agency's analysis may also cover short-term exposure effects. In the methylene chloride rule, for example, OSHA set the 8-hour TWA PEL primarily to reduce the risk of employees developing cancer, while the 15-minute short-term exposure limit (STEL) was primarily designed to protect against noncancer risks, such as negative effects on the central nervous system.

Finally, Rhomberg pointed out the following distinct features of occupational exposure assessments:

> Compared to environmental exposures, exposures in the workplace tend to be much better defined. The workplace is a confined setting within which practices and behaviors tend to be standardized. Exposure levels are often high enough to be easily measured, and many workplaces have ongoing monitoring of environmental levels of compounds.[16]

[16] Rhomberg (1996), p. 36.

Risk Assessment Assumptions and Methodological Choices

As previously noted, OSHA's risk assessment procedures, including its default assumptions and methodological preferences, tend to be established through the precedents of prior rulemakings. In contrast to EPA and FDA, OSHA also appears to choose somewhat less conservative options, even though the agency notes that Congress and the courts have permitted and even encouraged it to consider "conservative" responses to both uncertainty and human variability. The Supreme Court's Benzene decision, in particular, affirmed that "the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of over-protection rather than under protection."[16] On the other hand, OSHA explicitly stated in rulemakings that it takes various steps to be confident that its risk assessment methodology is not designed to be overly conservative (in the sense of erring on the side of overprotection). Although not intended to be comprehensive, table 8 illustrates some of the specific assumptions or methodological choices used by OSHA. It also illustrates the overt balancing of more and less conservative choices that characterizes OSHA's approach to risk assessment. The information presented in table 8 was taken primarily from OSHA risk assessment documents but also reflects additional comments provided by OSHA officials. (GAO notes and comments appear in parentheses.)

Table 8: OSHA Risk Assessment Assumptions and Methodological Choices

Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
1. Most things being equal, epidemiologic data are preferred to data from animal studies whenever good data on human risks exist.	Avoids the uncertainty of cross-species extrapolation. Also, most human studies on nondrug chemicals come from occupational exposures.	Choice of data set for quantitative cancer risk assessment (hazard identification and dose-response assessment)	(Not identified.)

[16] 448 U.S. at 656.

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Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
2. It is reasonable to suspect that substances that cause cancer in multiple animal species and at multiple target organ sites would be carcinogenic to humans. Therefore, OSHA relies on well-conducted, high-quality animal bioassays as the primary basis for cancer hazard identification and often for quantitative risk assessment.	Virtually all of the toxic substances that have been demonstrated to be carcinogenic in humans are also carcinogenic in laboratory animals.	Choice of data set for qualitative and quantitative cancer risk assessment (hazard identification and dose-response assessment) –in the absence of sufficiently powerful negative epidemiological studies or mechanistic studies demonstrating that the purported carcinogenic mechanism of action of the substance is irrelevant to humans.	(Not specifically identified, but OSHA did note that it is possible that a substance may be carcinogenic in a laboratory species but not in humans. OSHA officials also pointed out that, as part of its risk assessment, OSHA examines all relevant toxicity data to determine the appropriateness of relying on extrapolation from animal studies.)
3. If human (epidemiological) data are equivocal, or the epidemiologic study is not sufficiently sensitive to identify an increased risk predicted by a well-conducted animal bioassay, it is necessary to consider the animal data to protect workers from significant risk.	To protect workers from significant risk.	Analysis of epidemiological and animal data for quantitative cancer risk assessment (hazard identification and dose-response assessment) –when animal studies indicate a positive response to a particular chemical and epidemiological studies of exposures to the same chemical fail to exhibit a statistically significant increase in risk.	(Not identified.)
4. In the absence of pharmacokinetic information satisfying OSHA's criteria for acceptance of PBPK models, OSHA relies on a default mg/kg/day species conversion factor.	(Not identified.)	Choice of animal-to-human dose equivalence for quantitative risk assessment (dose-response assessment).	(Not identified, but this is generally considered to be a conservative approach.)
5. OSHA uses site-specific tumor incidence, rather than pooled tumor response, in determining the dose-response function for a chemical agent. OSHA estimates excess risks to humans based on the most sensitive species-sex-tumor site.	(Not explicitly identified. Per comments from OSHA it reflects, in part, a policy choice to be conservative, but not overly conservative.)	Choice of data set for quantitative cancer risk assessment (dose-response assessment).	OSHA cited this as an instance where the agency does not use the most conservative approach.

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Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
6. OSHA combines benign tumors with the potential to progress to malignancies with malignant tumors occurring in the same tissue and the same organ site.	Evidence suggests that such tumors should be interpreted as representing a potentially carcinogenic response. (In support of this position, OSHA cited the views of the Office of Science and Technology Policy on chemical carcinogenesis [citation provided]. OSHA also pointed out that other federal agencies—EPA, FDA, the Consumer Product Safety Commission, and the National Institute for Occupational Safety and Health—have also included benign responses in their assessments.)	Choice of data set for quantitative cancer risk assessment (dose-response assessment).	(Not specifically identified in the risk assessments we reviewed, but according to OSHA officials is almost always conservative.)
7. OSHA relies on low-dose extrapolation to estimate risks associated with exposure levels of interest; however, because occupational exposures are typically much higher than those encountered in the general environment, OSHA's risk assessments do not extrapolate as far beyond the range of observed toxicity as might be necessary to characterize environmental risks.	(Not explicitly identified, but the assumption that you can extrapolate low-dose effects from high-dose effects is a standard assumption of risk assessment.)	Dose-response assessment.	(Not identified.)

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Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
8. For low-dose animal-to-human cancer risk extrapolation, OSHA's preference is to use the maximum likelihood estimate (MLE) in the Crump-Howe reparameterization of the "multistage model." This model is based on the biological assumption that carcinogens induce cancer through a series of independent viable mutations in a series of stages, and that each mutation rate is linearly related to dose. The multistage model used by the agency also assumes no threshold for carcinogenesis.	OSHA stated that it believes that the multistage model conforms most closely to what is known about the etiology of cancer, including the fact that linear-at-low-dose behavior is expected for exogenous agents, which increase the risk of cancer already posed by similar "background" processes. OSHA noted that there is no evidence that the multistage model is biologically inappropriate, especially for genotoxic carcinogens, and that the overwhelming scientific consensus is that genotoxins follow low-dose linear functions. However, OSHA officials also pointed out that the Crump-Howe algorithm that OSHA uses can yield nonlinear models. OSHA's preference is consistent with the position of the Office of Science and Technology Policy, which recommended that "when data and information are limited, models or procedures that incorporate low-dose linearity are preferred when compatible with limited information" [citation provided].	Cancer dose-response assessment.	The multistage model is generally considered to be a conservative model because it is approximately linear at low doses and because it assumes no threshold for carcinogenesis, although there are other plausible models of carcinogenesis which are more conservative at low doses. (OSHA officials also pointed out that the algorithm that OSHA uses to compute MLE estimates is less conservative because it may lead to models that are sublinear at low doses.)
9. OSHA's default choice is to select the MLE of the parameterized dose-response function, rather than the upper 95-percent confidence limit.	In part, this appears to reflect a policy choice. OSHA cited this choice as one of the steps it has taken that make it fairly confident its risk assessment methodology is not designed to be overly "conservative," in the sense of erring on the side of overprotection.	Cancer dose-response assessment.	OSHA cited this as an instance where the agency does not use a conservative (or the most conservative) approach.

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Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
10. For interspecies dose scaling, OSHA assumes that equivalent doses in mg/kg/day (body weight scaling) would lead to equivalent risks. (OSHA's Director of Health Standards noted that the agency might also move to consideration of ¾-power scaling, as agreed to by EPA, FDA, and the Consumer Product Safety Commission, or to develop a probability distribution for the power.) In addition, to convert mg/kg/day doses to parts per million (ppm), OSHA uses a human breathing rate of 9.6 m^3/workday and human body weight of 70 kg.	In its risk assessments, OSHA points out that there are several plausible options for extrapolating human risks from animal data via interspecies scaling factors [citations provided]. OSHA states that its selection of body weight scaling is one of the steps it takes that make the agency fairly confident that its risk assessment methodology is not "conservative" in the sense of erring on the side of overprotection. (No particular basis cited for using the specific breathing rate and body weight figures, just that they are OSHA's preferred values.)	During dose-response assessment, when estimating the equivalent human dose based upon an experimental dose in animals.	OSHA notes that the body weight extrapolation approach that it generally uses tends to be significantly less conservative than other plausible methodologies and most likely is less conservative even than the central tendency of the plausible values. The agency also notes that, across the series of plausible values, its body weight extrapolation approach is generally considered the least conservative, $(body\ weight)^{2/3}$ [surface area scaling] the most conservative, and $(body\ weight)^{3/4}$ the midpoint value.
11. OSHA assumes that workers will be exposed to a chemical at the maximum permissible level for 45 years. The standard values used for assessing exposures over a working lifetime are: a. 45 years per working lifetime, b. 5 workdays per week, and c. 8 hours per workday.	The focus on working lifetime exposure comes from the statutory mandate under the OSH Act to protect an employee "even if such employee has regular exposure to the hazard... for the period of his working life." The choice of 45 years is based on a worker beginning work at age 20 and retiring at age 65.	Exposure assessment.	OSHA notes that this reflects a "more conservative" choice.

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Assumption or methodological choice	Reason(s) for selection	When the assumption/choice would be applied (step in the risk assessment process or circumstances)	Likely effect on risk assessment results
12. The general boundary within which acceptable versus unacceptable risk falls is between an insignificant fatality risk of one in one billion (10^{-9}) and a significant risk of 1 in one thousand (10^{-3}). More explicitly, OSHA stated in one of its rulemakings that risks at or above 10^{-3} (1 per 1000) are always significant by any empirical, legal, or economic argument available.	The general boundary is directly attributed to the Supreme Court's 1980 Benzene decision.	Policy for evaluating "significant risk."	(No direct effect on the risk estimates, but this general policy does serve as an underlying focus in conducting risk assessments.)

Source: Compiled from GAO review of OSHA risk assessment documents and from additional comments provided by agency officials.

Risk Characterization

Although OSHA does not have written risk characterization policies, recent OSHA rulemakings showed that the agency emphasized (1) comprehensive characterizations of risk assessment results; (2) discussions of assumptions, limitations, and uncertainties; and (3) disclosure of the data and analytic methodologies on which the agency relied. Rhoinberg noted that OSHA's usual practice is to present the results and methodological bases of outside parties' risk assessments for a chemical in addition to OSHA's own assessment, and to feature several possible bases for risk calculation in its characterization of risks. In checking examples of recent OSHA rulemakings, we also observed this emphasis on showing a range of alternative assessments, both those of external parties and OSHA's own sensitivity analyses.

At least three factors help to explain this proclivity to characterize risks using different data sets, assumptions, and analytical approaches, all of which are rooted in the statutory context for OSHA standards setting. First, the agency's statutory mandate, reinforced by the Supreme Court's Benzene decision, is that it must demonstrate "significant" risk from workplace exposure to a chemical with "substantial evidence." Second, the OSH Act directs OSHA to base health standards on the "best available